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SECTION Brain, Spinal Cord, and Nerve Disorders

SUBJECT Infections of the Brain and Spinal Cord

Viral Infections

Viral infections can produce inflammation of the meninges (causing viral meningitis), the brain (causing viral encephalitis), the spinal cord (causing myelitis), or spinal nerve roots (causing shingles). Viral encephalitis is often accompanied by viral meningitis. Viral encephalitis is more serious because it directly affects the brain rather than the meninges.

Some viruses can directly infect the brain and suddenly cause encephalitis. Infections due to some viruses, such as echovirus or coxsackievirus, can occur in epidemics. Other infections (such as herpes, mumps, and chickenpox) occur as isolated cases (sporadically). Rabies encephalitis, which is fatal, results from being bitten by an animal (such as a bat). Infections called arbovirus encephalitis are spread by mosquitoes, ticks, or other arthropods. Other viral infections, such as lymphocytic choriomeningitis, are spread by rodents. The human immunodeficiency virus (HIV) produces a chronic infection of the brain without the inflammation that occurs in acute encephalitis; this disorder is called HIV encephalopathy or AIDS dementia.

Some viruses do not directly infect the brain; instead, they trigger immune reactions that indirectly result in inflammation of the brain. This type of inflammation, which is called parainfectious or postinfectious encephalitis, can follow measles, chickenpox, or rubella, typically developing 5 to 10 days later. It can cause severe damage. The spinal cord may also be affected, resulting in acute disseminated encephalomyelitis (see Multiple Sclerosis and Related Disorders: Other Primary Demyelinating Diseases).

Very rarely, encephalitis develops weeks, months, or years after a viral infection. An example is subacute sclerosing panencephalitis, a brain inflammation that occasionally follows measles. This disorder most commonly occurs in children (see Viral Infections: Subacute Sclerosing Panencephalitis).

Symptoms

Some viral infections are mild, causing fever and a general feeling of illness (malaise), often without specific symptoms. Usually, viral meningitis produces symptoms that are similar to those of bacterial meningitis (fever, headache, vomiting, weakness, and a stiff neck) but that are much less severe.

Viral encephalitis can cause personality changes, seizures, paralysis of the limbs, confusion, and sleepiness that can progress to coma and death. In its early stages, encephalitis due to the herpes simplex virus (herpes encephalitis)—a treatable but potentially fatal infection—causes headache, fever, and flu-like symptoms. It also causes symptoms that indicate inflammation of the temporal lobes. They include seizures that usually involve strange smells, vivid flashbacks, or experience of a sudden, intense emotion. When this infection progresses, it causes severe brain damage resulting in confusion, repeated seizures, or coma.

When viral infections affect the spinal cord, the first symptom may be back pain at the site of the infection. Depending on which level of the spinal cord is affected (see Which Area of the Spine Is Damaged?), the parts of the body supplied by the spinal cord below that level may feel numb and weak. Bladder and bowel function may be impaired. If the infection is severe, sensation may be lost, paralysis may occur, and bladder and bowel control may be lost.

Diagnosis

At first, doctors may have difficulty distinguishing viral meningitis and encephalitis from bacterial meningitis, abscesses in the brain, and other disorders that cause similar symptoms. At the first sign of any of these disorders, doctors try to pinpoint the cause. A spinal tap to examine the cerebrospinal fluid is almost always performed. In viral infections, the number of white blood cells is increased in the cerebrospinal fluid, and no bacteria are seen. Red blood cells are absent unless the inflammation is severe. Immunologic tests that detect antibodies against viruses in samples of cerebrospinal fluid may be performed, but these tests take days to complete. Even with these tests, a specific microorganism is identified less than half the time. Culturing most viruses from the fluid is difficult and takes many days; therefore, the fluid is rarely sent to be cultured. Polymerase chain reaction (PCR) techniques are used to identify organisms such as herpes viruses.

Doctors suspect herpes encephalitis when the case is not part of an epidemic and when symptoms indicate inflammation of the temporal lobes. Magnetic resonance imaging (MRI) can detect increased swelling in the temporal lobes and thus can help doctors make a quick diagnosis. Computed tomography (CT) is less helpful because it usually detects changes only after severe damage has occurred. When herpes encephalitis is severe (as it ultimately becomes), the cerebrospinal fluid contains many red blood cells. Occasionally, a biopsy of brain tissue (in which a tissue sample is removed for examination under a microscope) is needed to determine whether the herpes simplex virus is the cause.

CT or MRI is also performed to rule out a brain abscess, stroke, or another structural disorder, such as a hematoma, an aneurysm, or a tumor, which may cause similar symptoms.

Treatment and Prognosis

If a viral infection causes only headache and fever, the only treatment usually required is acetaminophen, given by mouth, and fluids, given by mouth or intravenous injection. Viral meningitis and many cases of mild viral encephalitis often resolve on their own and require no specific treatment.

For some severe viral infections, certain antiviral drugs are effective. For people with herpes encephalitis, prompt treatment with the antibiotic acyclovir is life-saving. If the diagnosis is in doubt, acyclovir is usually given because the herpes simplex virus is the cause in up to one third of people with encephalitis. Acyclovir is effective against herpes simplex and herpes zoster but not against most other viruses. Ganciclovir is effective against cytomegalovirus. For other infections, no specific treatment is available. Treatment involves relieving symptoms and, when necessary, providing life support.

What Is Aseptic Meningitis?

"Aseptic" is a term doctors may use to describe meningitis when no bacteria are identified during routine testing. Aseptic meningitis may be caused by noninfectious disorders, such as leukemia, lymphoma, or brain cancer, or by the use of certain drugs, such as chemotherapy drugs injected directly into the cerebrospinal fluid, drugs used to prevent rejection of transplanted organs (immunosuppressants), and even nonsteroidal anti-inflammatory drugs (NSAIDs). However, in most cases, a virus is the cause. Consequently, doctors often use aseptic meningitis and viral meningitis as synonyms.

Aseptic meningitis may be brief (acute)

For HIV infection, a combination of drugs (see Drugs For HIV Infection) helps the immune system function better and delays the progression of the infection and its complications, including dementia.

or prolonged (chronic). It is usually mild and does not require treatment. Rarely, it can be severe and life threatening.

Many people recover completely. The chances of survival and recovery depend largely on the type of virus and the promptness of treatment if available. For example, people who have encephalitis due to the herpes simplex virus must be treated with acyclovir before they lapse into a coma if they are to recover well. Infants are more likely to have permanent damage.

RABIES

Rabies is a viral infection of the brain that is transmitted by animals and causes inflammation of the brain and spinal cord.

Usually, rabies is eventually fatal once the rabies virus reaches the spinal cord and brain, but the virus takes at least 10 days—usually 30 to 50 days—to reach the brain (depending on where the bite is). During that interval, measures can be taken to eradicate the virus and help prevent death.

The rabies virus is present in many species of wild and domestic animals throughout most of the world. Animals with rabies may be sick for several weeks before they die. During that time, they often spread the disease.

The rabies virus, which is present in the saliva, is transmitted when a rabid animal bites or, very rarely, licks another animal or a person. The virus cannot pass through intact skin and can enter the body only through a puncture or another break in the skin. In the United States, almost all cases of rabies in people have been spread by bats but with no evidence of a bite, suggesting that the virus was probably inhaled.

From the point of entry, the virus travels along nerves to the spinal cord and then to the brain, where it multiplies. From there, it travels along other nerves to the salivary glands and into the saliva.

Many different animals—such as cats, bats, raccoons, skunks, and foxes as well as dogs, the most common source—can transmit rabies to people. Rabies rarely affects rodents (such as mice, rats, hamsters, and squirrels), rabbits, or hares. In the United States, these animals have not been known to cause rabies among people. Birds and reptiles do not develop rabies. In the United States, vaccination has largely eliminated rabies in dogs. Worldwide, during the last 30 years, most people who have contracted rabies were bitten by rabid wild animals. However, rabies in dogs is still fairly common in most countries of Latin America, Africa, and Asia, where vaccination of dogs is not widespread.

Rabies has a furious and a dumb form. An animal with furious rabies is agitated and vicious, then becomes paralyzed and dies. An animal with dumb rabies is partially or generally paralyzed from the beginning. However, wild animals with furious rabies are less likely to appear vicious. Changes in their behavior are usually more subtle. For example, nocturnal animals (such as bats, skunks, raccoons, and foxes) may come out during the day and may not show normal fear of people.

Symptoms

Symptoms appear when the rabies virus reaches the brain or spinal cord, usually 30 to 50 days after the person is bitten. However, this interval can vary from 10 days to more than a year. The

closer the bite to the brain, the more quickly symptoms appear.

Rabies commonly begins with a short period of depression, restlessness, a general feeling of illness (malaise), and a fever. However, in 20% of people, rabies begins with paralysis in the lower legs that moves up through the body. Restlessness increases, leading to uncontrollable excitement, and saliva production greatly increases. Spasms of the muscles in the throat and voice box occur because rabies affects the area in the brain that controls swallowing and breathing. The spasms can be excruciatingly painful. A slight breeze or an attempt to drink water can trigger the spasms. Thus, a person with rabies cannot drink. For this reason, the disease is sometimes called hydrophobia (fear of water).

As the disease spreads through the brain, the person becomes more and more confused and very agitated. Eventually, coma and death result. The cause of death can be blockage of airways, seizures, exhaustion, or widespread paralysis.

Diagnosis

When a person is bitten by a pet that appears sick or by a wild animal, the biggest concern is rabies. No test can determine whether the rabies virus has been transmitted to the person immediately after the bite. So the animal is evaluated to determine whether the person requires treatment. A wild animal that has bitten a person is killed if possible, and a pet that appears sick is taken to the veterinarian to be put to sleep (euthanized), so that its brain can be examined for signs of rabies. Certain pets—dogs, cats, and ferrets—that do not appear sick may be confined and observed by a veterinarian for 10 to 14 days. If the pet remains healthy, it did not have rabies at the time of the bite. For other pets that appear healthy, the veterinarian or public health officials should be consulted.

If a person who has been bitten by an animal becomes increasingly confused and agitated or paralyzed, the diagnosis is probably rabies. At this point, tests can detect the rabies virus. A skin biopsy, in which a sample of skin is taken (usually from the neck) for examination under a microscope, can detect the virus.

Prevention and Treatment

The first step in prevention is to avoid being bitten by animals, especially wild animals. Pets that are not known and wild animals should not be approached. A wild animal that does not appear afraid of people is usually sick. An animal that appears sick should not be picked up to try to help it. A sick animal often bites.

People who are at high risk of exposure to the rabies virus should be given an injection of the rabies vaccine before exposure. High-risk people include veterinarians, laboratory workers who handle animals that may be rabid, people who live or stay more than 30 days in developing countries where rabies in dogs is widespread, and people who explore bat caves. Vaccination protects most people to some degree for the rest of their life. However, protection decreases with time, and people at high risk of continued exposure should receive a booster dose of vaccine every 2 years.

If a person is bitten by a rabid animal, the development of rabies can usually be prevented if appropriate measures are taken without delay.

The bite wound is treated immediately. It is cleaned thoroughly with soap and water. Deep puncture wounds are flushed out with soapy water. Sometimes doctors trim tissue from the edges of the wound.

People who have not been previously immunized with rabies vaccine may be given an injection of rabies immunoglobulin, depending on the status of the animal. Rabies immunoglobulin, which consists of antibodies against the virus, provides protection immediately but only for a short time. Several injections of rabies immunoglobulin are given initially (day 0), followed by injections of the rabies vaccine on days 3, 7, 14, and 28. Rabies vaccine stimulates the body to produce antibodies against the virus, providing protection that begins more gradually but that lasts for a much longer time than the protection provided by rabies immunoglobulin. Pain and swelling at the injection site are usually minor. Serious allergic reactions are rare.

If a person who is bitten has already been vaccinated, the risk of developing rabies is reduced. However, the wound must be cleaned promptly and an injection of rabies vaccine is given immediately and 2 days later (on day 3).

After a person develops symptoms, neither rabies vaccine nor rabies immunoglobulin is effective against the virus. Treatment is then directed at relieving symptoms and making the person as comfortable as possible. Death almost always results.

ARBOVIRUS ENCEPHALITIS

Arbovirus encephalitis is a severe inflammation of the brain caused by one of a group of viruses transmitted by certain arthropods, such as mosquitoes and ticks.

In the United States, the most common types of viral encephalitis are caused by arboviruses. Arboviruses are transmitted to people through the bite of mosquitoes, ticks or other arthropods. (Arbovirus is short for *ar*thropod-*bo*rne *virus*.) The viruses are transmitted to the arthropods when the arthropods bite infected animals. Many species of domestic animals and birds carry these viruses. Epidemics occur in people only periodically—when the population of mosquitoes or infected animals increases. Infection spreads from arthropod to person, not from person to person.

Many arboviruses can cause encephalitis. The different types of encephalitis that result are usually named for the place the virus was discovered or the animal species that typically carries it.

Several types of arbovirus encephalitis occur in the United States. All of the following are spread by mosquitoes. **Western equine encephalitis** occurs throughout the United States. It affects all age groups, but mainly children younger than 1 year. **Eastern equine encephalitis** occurs predominantly in the eastern United States. It affects mainly young children and people older than 55. The eastern type is more likely to be fatal than the western type. Both types tend to cause severe symptoms in children younger than 1 year, causing permanent nerve or brain damage. **St.**

Who Should Receive a Rabies Vaccine?

The decision to administer the rabies vaccine to a person who has been bitten by an animal depends on the type and status of the animal.

For people bitten by a pet dog, cat, or ferret:

If one of these animals appears healthy and can be observed for 10 days, the vaccine is not given unless the animal develops symptoms of rabies. If the animal develops any symptom suggesting rabies, the vaccine is given immediately. Animals that develop symptoms of rabies are put to sleep (euthanized), and their brain is examined for the rabies virus.

If one of these animals has or appears to have rabies, the person who has been bitten is given the vaccine immediately.

If the status of one of these animals cannot be determined—for example, because it escaped, public health officials are consulted to determine what the likelihood of rabies is and whether the vaccine should be given.

For people bitten by skunks, raccoons, foxes, most other carnivores, or bats:

Such an animal is considered rabid unless it can be tested and the results

Louis encephalitis occurs throughout the United States, but particularly in Texas and some midwestern states. The risk of death is greatest in older people. Several related viruses cause **California encephalitis,** which affects mainly children. These viruses include the California virus (most common in the western United States), the La Crosse virus (most common in the midwestern United States), and the Jamestown Canyon virus (commonly in the area around the Great Lakes). **West Nile encephalitis,** once present only in Europe and Africa, first appeared in the New York City area in 1999. By 2000, cases were reported along the East Coast from Vermont to North Carolina. Several species of birds are the host for the virus. This encephalitis affects mainly older people. About 1 of 10 infected people die.

In other parts of the world, encephalitis is caused by different but related arboviruses. Examples are Venezuelan equine encephalitis and Japanese encephalitis, both spread by mosquitoes.

are negative. The person who has been bitten is usually given the vaccine immediately. Waiting to observe wild animals for 10 days is not recommended.

For people bitten by livestock, small rodents, large rodents (such as woodchucks and beavers), rabbits, or hares:

Each biting incident is considered individually, and public health officials are consulted. People who are bitten by squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice, other small rodents, rabbits, and hares almost never require rabies vaccination.

Symptoms and Diagnosis

The different types of arbovirus encephalitis produce similar symptoms. Usually, the first symptoms include headache, drowsiness, and fever. Vomiting and a stiff neck are less common. Muscles may tremble. Confusion, seizures, and coma may develop rapidly. Occasionally, the arms and legs become weak or paralyzed.

Arbovirus encephalitis is suspected on the basis of symptoms, especially if an epidemic is in progress. To confirm the diagnosis, doctors take a sample of blood or cerebrospinal fluid and test it for antibodies against the virus when the person is sick and later when the person is convalescing. If the test detects a marked increase in the level of antibodies, the diagnosis is confirmed. Alternatively, polymerase chain reaction (PCR) techniques, which cause DNA to make copies of itself, can be used to detect the genetic material of the virus.

Prevention and Treatment

The best way to prevent the encephalitis is to control the mosquitoes that spread it. Also, taking precautions against being bitten can help: using insect repellents, wearing a long-sleeve shirt and long pants, and avoiding standing water, where the mosquitoes can breed. No vaccines against arboviruses are available.

No specific treatment is available. Treatment usually involves relieving symptoms and, when necessary, providing life support until the infection subsides—in about 1 to 2 weeks.

Lymphocytic Choriomeningitis

Lymphocytic choriomeningitis is a flu-like disorder caused by an arenavirus and often followed by meningitis.

The arenavirus that causes lymphocytic choriomeningitis is commonly present in rodents, especially the gray house mouse and the hamster. These animals are usually infected by the virus for life and excrete it in urine, feces, semen, and nasal secretions. Most often, exposure to dust or food contaminated by these waste products causes the disorder in people. The disorder

usually occurs in winter when wild rodents seek shelter indoors.

Symptoms

The disorder often occurs in two phases. In the first phase, flu-like symptoms develop 5 to 10 days after exposure to the virus. A fever of 101 to 104° F (38.3 to 40° C) typically occurs and may be accompanied by shaking. Other symptoms include a general feeling of illness (malaise), nausea, light-headedness, weakness, muscle pains, a headache behind the eyes worsened by bright light, and a poor appetite. Sore throat may occur, and sensitivity to touch may be reduced.

After 5 days to 3 weeks, the flu-like symptoms may subside for 1 or 2 days. In the second phase of the disorder, these symptoms recur and other symptoms develop. Other symptoms may include painful and swollen finger joints, inflammation of the testes, loss of hair, and vomiting. Meningitis may develop, causing a headache and stiff neck. Most people who develop meningitis recover completely. Occasionally, encephalitis develops, causing a headache and drowsiness. Rarely, some symptoms persist because of brain damage due to encephalitis.

Diagnosis and Treatment

At first, the disorder cannot be distinguished from the flu, so usually no tests are performed. If symptoms suggest meningitis, a spinal tap is performed to obtain a sample of the cerebrospinal fluid. If lymphocytic choriomeningitis is present, the cerebrospinal fluid usually contains many white blood cells, mostly lymphocytes. The disorder is diagnosed by identifying the virus in the cerebrospinal fluid or by detecting increasing levels of the antibody against the virus in the blood.

No specific treatment is available. Doctors try to relieve the symptoms until the disorder subsides—in about 1 to 2 weeks.

PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

Progressive multifocal leukoencephalopathy is a rare infection of the brain and spinal cord that is caused by the JC virus.

Progressive multifocal leukoencephalopathy results from infection by the JC virus. The disorder affects mainly people whose immune system is impaired, such as people who have leukemia, lymphoma, or AIDS, or is suppressed by use of immunosuppressants, which may be used to prevent rejection of transplanted organs or to treat autoimmune disorders. About 4% of people with AIDS have this disorder.

Symptoms and Diagnosis

Many people who are infected with the JC virus have no apparent symptoms. The JC virus appears to remain inactive until something (such as an impaired immune system) allows it to be reactivated and start to multiply.

Symptoms vary depending on which part of the brain or spinal cord is infected. Symptoms may begin gradually, but they usually worsen rapidly. Paralysis commonly affects one side of the body. The hands rapidly become clumsy, making writing and grasping objects difficult. In about two of three people, mental function declines rapidly and progressively, causing dementia. Speaking becomes increasingly difficult, and partial blindness is characteristic. Rarely, headaches and seizures occur. Death is common within 1 to 6 months of when symptoms start, but a few people survive longer (about 2 years). Even fewer people improve for a few months and survive for up to 10 years.

Progressively worsening symptoms in a person with a severely impaired immune system suggest the diagnosis. Noninvasive procedures, such as computed tomography (CT) and magnetic

resonance imaging (MRI), can help establish the diagnosis. However, the diagnosis is often not confirmed until after the person has died, when brain tissue can be examined. Polymerase chain reaction (PCR) techniques, which cause DNA to make copies of itself, can detect the JC virus in the cerebrospinal fluid of up to 90% of people.

Treatment

No treatment of progressive multifocal leukoencephalopathy has proved effective. However, longer survival results from treating the disorder that has impaired the immune system. Such treatment includes highly active antiretroviral therapy (antiviral drugs used to treat AIDS). Discontinuing immunosuppressants can cause progressive multifocal leukoencephalopathy to subside.

TROPICAL SPASTIC PARAPARESIS

Tropical spastic paraparesis is a slowly progressive viral infection of the spinal cord that causes weakness in the legs.

Tropical spastic paraparesis (also called HTLV-associated myelopathy) affects nerve bundles inside the spinal cord. The myelin sheath (which surrounds the part of the nerve that sends messages) is damaged or destroyed (demyelinated). This disorder results from infection by the human T-cell lymphotropic virus type I (HTLV-I). This virus, a retrovirus, can also cause a type of leukemia. Tropical spastic paraparesis may be transmitted through sexual contact or contaminated needles. It can also be transmitted from mother to child across the placenta or in breast milk.

Symptoms may begin years after exposure to the virus. Symptoms develop when the immune system damages nerve tissue in the process of responding to infection with HTLV-I. Muscles in both legs gradually become weak and stiff. These symptoms worsen over several years. Some sensation in the feet may be lost. Urinary problems, including frequent, strong urges to urinate and incontinence, are common. Bowel dysfunction may occur.

No cure is available. However, use of corticosteroids has produced marked improvement, and plasmapheresis has produced temporary improvement.

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